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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,549	04/01/2002	Michio Kubota	KUBOTA=9	3265

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EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 05/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,549	KUBOTA ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,8-15,43 and 46-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,8-15,43 and 46-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some* c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1-19-05 and 3-5-05 has been entered.

Claims 1, 3, 8-15, 43, 46-47, 48-51 are currently pending and are present for examination.

Applicants' amendments and arguments filed on 3-5-05, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Specifically Examiner has withdrawn few of the rejections under 35 U.S.C. 112, 2nd paragraph in view of claim amendments. Examiner has also withdrawn the rejection under 35 U.S.C. 112, Ist paragraph for lack of biological deposit certification in view of the certification now provided by the applicant.

Sequence Compliance

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that applicants fail to provide SEQ ID NOs for amino acid sequences recited in pages 33, 87, 88; 89, 103, 105 (in tables). Examiner urges applicants to provide appropriate

SEQ ID NO for sequences in the above pages and wherever such sequences are recited in the specification. See particularly 37 CFR 1.821(d).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and claims 3, 8-15, 43, 46-47, 51 which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites two different molecular weights for the claimed enzymes and provides sometimes two values and some times three values for other characteristics such as isoelectric point, optimum temperature, optimum pH etc. It is not clear to the Examiner as to which enzyme with a specific molecular weight (for example 140,000 daltons) has which value with respect to the other characteristics such as isoelectric point, optimum temperature, optimum pH etc. It is not clear whether all the enzymes have all the characteristics or whether specific enzyme with a specific molecular weight has a specific value for other characteristics such as isolelectric point, optimum temperature, optimum pH etc.

Claim 43 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 43 recites the phrase "derived from a microorganism". The metes and bounds of this phrase is not clear to the Examiner. Literally, while the term "derived" means "to

isolate from or obtain from a source", the above term could also mean "to arrive at by reasoning i.e., to deduce or infer" or also mean "to produce or obtain from another substance". Therefore, it is not clear to the Examiner either from the specification or from the claims as to what applicants mean by the above phrase. It is not clear to the Examiner whether the "derived from a microorganism..." encompasses a single microorganism, i.e., a specific bacteria such as Bacillus globisporus C-9 or whether it encompasses recombinants, variants and mutants of any microorganism including all or any bacteria, fungi, protozoa and algae. As applicants have not provided a definition for the above phrase, Examiner has interpreted the claims broadly to mean, that the claimed enzyme in claims 43 and 49 "derived from a microorganism..." encompasses said enzymes isolated from all or any microorganism including all or any bacteria, fungi, protozoa and algae. Examiner has given the same interpretation while considering the claims for all other rejections. Examiner suggests the use of the phrase "isolated from" in order to overcome this rejection.

Claim 51 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 51 recites the phrase "substantially incapable of". The metes and bounds of this phrase is not clear to the Examiner. A perusal of the specification did not yield a specific definition for the above phrase. Therefore, without a specific definition it would be unclear to those skilled in the art as to how much of a reduction in dextran forming ability of said enzyme is considered as "substantial" by the applicants.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter (new matter) which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1, 48 and claims 3, 8-15, 43, 46-47, 49-51 which depend therefrom are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1, 48 are drawn to isomaltosylglucosaccharide synthase polypeptides having various characteristics such as molecular weight, temperature optimum, pH ranges etc., none of which match with the characteristics described in the specification. For example, in claim 1, the enzyme claimed has a molecular weight of 140,000 $\pm$ 20,000 or 137,000 $\pm$ 20,000 and an isoelectric point of 5.2 $\pm$ 0.5 or 7.3 $\pm$0.5. Applicant indicates that said amendment has support in example 5-1 on p 69, Example 8-1 on page 81 and Example 12-1 on page 97. A perusal of said pages indicates that the molecular weights of the enzyme does not match with the isoelectric point of the enzyme. While the enzyme with the molecular weight 140,000 $\pm$ 20,000 has indeed an isoelectric point of 5.2 $\pm$ 0.5, the enzyme with molecular weight 137,000 $\pm$ 20,000 does not have said isoelectric point, but it is the enzyme with molecular weight 136,000 $\pm$ 20,000 in example 12-1 on page 97 that has an isoelectric point of 7.3 $\pm$0.5.

Similarly, applicants remark that the support for the enzyme now claimed in claim 48 can be found at page 32, lines 6-10 and even provides a recitation from the specification. However upon careful perusal of the specification, those characteristics are only part of the characteristics described for an enzyme having a molecular weight in the range of 74,000 to 160,000 (see page 31). Therefore there is no specific support for an enzyme with a molecular weight 94,000 $\pm$ 20,000 with an isoelectric point of 4.3 $\pm$ 0.5 as claimed in claim 48 at page 32. Applicants appear to pick and choose characteristics of enzymes from a list recited in the specification. Such characteristics claimed now constitutes a "new matter" since applicants do not have appropriate support in the specification. Therefore claims 1, 48 and 3, 8-15, 43, 46-47, 49-51 which depend therefrom are rejected for introducing "new matter" into the claims.

In response to the previous Office action, applicants assert that there is support for the claimed inventions. However, as explained above, applicants have picked and chosen specific characteristics from different enzymes and when the invention considered as a whole it lacks appropriate support in the specification. Applicants also argue that Table 7 on page 82 and Table 19 in page 113 is a typographical error and have made no attempt to correct the same. Next applicant also remarks that claim 1 has been amended to recite three molecular weights. However, claim 1 recites only two molecular weights, 140,000 $\pm$ 20000 or 136,000 $\pm$ 20,000. There is no recitation of 136,000 $\pm$ 20000 as argued in the remarks. Hence the above rejection is maintained.

Claims 1, 3, 8-15, 43, 46-47, 48-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isomaltosylglucosaccharide-forming

enzyme (IMG) isolated from *Bacillus globisporus C9,* FERM BP-7143, *Bacillus globisporus C11,* FERM BP-7144, *Bacillus globisporus N75,* FERM BP-7590 or *Arthrobacter globiformis A19,* FERM BP-7590, wherein said enzyme comprises either SEQ ID NO:1, 11 or 18, and wherein said enzyme forms a saccharide having a glucose polymerization degree of at least three with both, an α-1,6-glucosidic linkage (as a linkage at the non-reducing end) and the α 1,4-glucosidic linkage (other than the linkage at the non-reducing end) by catalyzing the α glucosyl transfer from a saccharide having glucose polymerization of at least two and having α 1,4-glucosidic linkage as a linkage at the non-reducing end, does not reasonably provide enablement for any such enzyme isolated from any or all sources such as any microorganism including any species of Bacillus or Arthrobacter or any bacteria, fungi, algae or protozoa or recombinants, mutants and variants of said enzymes having a broad molecular weight range and characteristics as claimed in claims 1 and 48. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1, 3, 8-15, 43, 46-47, 48-51 are so broad as to encompass any IMG from any or all sources such as any microorganism including any species of *Bacillus* or *Arthrobacter* or any

bacteria, fungi, algae or protozoa or recombinants, mutants and variants of said enzymes having a broad molecular weight range and characteristics as claimed in claims 1 and 48. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of IMG's broadly encompassed by the claims including all such enzymes from any microorganism and all such enzymes which are variants, mutants and recombinants of the same. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the specific enzymes isolated from *Bacillus globisporus C9,* FERM BP-7143, *Bacillus globisporus C11,* FERM BP-7144, *Bacillus globisporus N75,* FERM BP-7590 or *Arthrobacter globiformis A19,* FERM BP-7590, wherein said enzyme comprise SEQ ID NO:1, 11, or 18 and wherein said enzyme forms a saccharide having a glucose polymerization degree of at least three with both, an α-1,6-glucosidic linkage (as a linkage at the non-reducing end) and the α 1,4-glucosidic linkage (other than the linkage at the non-reducing end) by catalyzing the α glucosyl transfer from a saccharide having glucose polymerization of at least two and having α 1,4-glucosidic linkage as a linkage at the non-reducing end. It would require undue experimentation of the skilled artisan to make and use the polypeptides as claimed by the applicants. The specification is limited to teaching the use of a polypeptide isolated from *Bacillus globisporus C9,* FERM BP-7143, *Bacillus globisporus C11,* FERM BP-7144, *Bacillus globisporus N75,*

FERM BP-7590 or *Arthrobacter globiformis A19,* FERM BP-7590 comprising SEQ ID NO:1, 11 or 18 as an IMG, but provides no guidance with regard to the making of variants and mutants or with regard to methods of isolating it from any or all sources. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any or all IMG isolated from any source including recombinants, mutants and variants and having a broad molecular weight ranging from 94,000 to about 140,000 Daltons because the specification does not establish: (A) a rational and predictable scheme for isolation of any IMG from any

source having a broad molecular weight ranging from 94,000 to about 140,000 Daltons; (B)regions of the protein structure which may be modified without affecting IMG activity; (C) the general tolerance of IMG polypeptides to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any amino acid residue in a polypeptide comprising SEQ ID NO:1, 11 or 18 with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including IMGs from all or any sources or with an enormous number of amino acid modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of IMGs having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicant has traversed the above rejection arguing argue that the rejection under 35 U.S.C. §112, first paragraph is not proper because Experiment 5-1 on pages 69-71, Experiment 8-1 on pages 81-83, Experiment 12-1 on pages 97-99 and Experiment on pages 112-114 provide enablement for the subject matter as recited in amended claim. Examiner respectfully disagrees with such an argument. This is because while the examples provide support for isolation of specific enzymes from specific microbial sources, it does not provide enablement for isolating said enzymes from any or all

sources or for making any or all types of variants, mutants, or recombinants. Furthermore, while methods to produce variants of a known polypeptide sequence such as site-specific mutagenesis, random mutagenesis, etc. and methods of culturing are well known to the skilled artisan producing variants as claimed by applicants (without any indication of conservative and consensus sequences and amino acid residues that can be modified without altering the function of the polypeptide) requires that one of ordinary skill in the art know or be provided with guidance for culturing and isolation of said enzyme from all sources and as well as the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of isolating and testing or producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. Therefore the above rejection is maintained.

Claims 1, 3, 8-15, 43, 46-47, 48-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 3, 8-15, 43, 46-47, 48-51 are directed to a genus of IMG comprising a specific 9-10 amino acid long peptide sequences (SEQ ID NO:1, 11, or 18). As discussed in the written

description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification fails to describe any other representative species by sufficient identifying characteristics (i.e., considerable amino acid sequence information) or properties to show that applicant was in possession of the claimed genus. The identifying characteristics recited in claims 1, 3, 8-15, 43, 46-47, 48-51 constitutes a minor aspect of the structural description-- does not include sufficient characteristics to limit the claimed genus to proteins which are not highly variable in both structure and function and the so called structural characteristics includes a wide variation in values for those characteristics that are recited. Furthermore, the claims include species in which a large percent of the amino acid sequence (depending on the total number of amino acids in the polypeptide) of the single disclosed species has been substituted as well as allowing alterations in functional characteristics such as substrate specificity, temperature optima, pH optima, and inhibitor/activator profiles. Therefore, the species within the genus are highly variable in both structure and function. While claim 1 has some characteristics as the limitations of the genus (i.e., having SEQ ID NO:1, 11or 18) these

characteristics, by themselves are not sufficient to change the fact that the claims include proteins which are highly variable in both structure and function because of wide variations in the values associated with those characteristics. Thus for all the reasons discussed, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office action, applicant has traversed the above rejection arguing that the claims have now been amended to recite SEQ ID NO and therefore the claimed invention is amply described. Examiner respectfully disagrees with such an argument and amendment to be persuasive to overcome the above rejection. This is because, the SEQ ID NO provided refers to short fragment or peptide of the enzyme and does not represent the full length sequence. Hence the above rejection is maintained.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura

Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

May 11, 2005